

the development of a stress response, increase cardiac morbidity, and prolong hospital stays.

New analgesic agents have led to improvements in acute pain management. The recent approval of ketorolac tromethamine, a potent nonsteroidal anti-inflammatory agent, has provided physicians with a nonopioid alternative for the treatment of mild to moderate pain and a useful adjunct to decrease the opiate requirement of moderate to severe pain. Possible advantages include the lack of sedation, respiratory depression, or disturbance of bowel and bladder function. Unfortunately, the use of ketorolac may be associated with serious side effects, including gastrointestinal ulceration, platelet dysfunction, and nephrotoxicity. Patients who are hypovolemic or have preexisting renal insufficiency may be particularly vulnerable to the nephrotoxicity.

Even more important than the introduction of new analgesic agents has been the increased use of regional anesthetic techniques and the development of better methods of drug delivery, particularly patient-controlled analgesia and the spinal administration of narcotics. Although narcotics (fentanyl citrate) may also be administered transdermally, this route is not well suited for the initial treatment of acute postoperative pain because 12 to 24 hours are required to reach a steady state. Transdermal administration, however, appears to have a useful role in the treatment of patients who, after several days, still cannot take anything orally and have relatively stable pain.

Numerous surveys have documented that scheduled or patient-requested, intermittent, intramuscular administration of narcotics fails to control postoperative pain. Patient-controlled analgesia effectively circumvents problems of variable absorption and delays. When in pain, the patient depresses a button, causing the delivery of a fixed intravenous dose from an infusion pump. The physician sets both the dose of drug delivered by the machine and the "lockout" interval, which is the time after a dose during which a second dose cannot be delivered by the machine. The "lockout" should be of sufficient duration to allow the patient to obtain near-peak effect from the dose already received, thereby safeguarding against overdosage due to cumulative effects. Along with administration based on patient demand, a low-dose continuous or basal infusion can be provided. The theory is that supplementation with a basal infusion should provide more effective pain control and encourage uninterrupted sleep; unfortunately, although the data are somewhat equivocal, they do not appear to confirm these benefits. In addition, the inclusion of a basal infusion may decrease the relative safety of the technique. Most studies document improved control of pain with patient-controlled analgesia. Moreover, patient acceptance is exceptionally high; in fact, in one controlled study, the use of patient-controlled analgesia resulted in greater patient satisfaction than the epidural administration of morphine sulfate, even though patients receiving epidural morphine had better analgesia.

Unlike the administration of systemic narcotics, the spinal administration of opiates can produce profound analgesia without a significant depression of the sensorium. Selective spinal analgesia can be achieved using either epidural or intrathecal opioid administration, but the use of an epidural catheter technique permits continuous or repeated injections to provide analgesia for prolonged periods and allows for the substitution or addition of local anesthetics. Although clinical management is more complex when local anesthetics are

combined with spinal opioids, the combination can increase analgesia, delay tachyphylaxis, and reduce the side effects that occur when either technique is used alone.

The importance of aggressive postoperative pain management has been underscored by the recent publication of clinical practice guidelines for acute pain management by the Agency for Health Care Policy and Research. The guidelines stress a collaborative interdisciplinary approach; an individualized plan developed preoperatively; assessment and frequent reassessment of the patient's pain; the use of both drug and nondrug therapies; and a formal institutional approach, including incorporating a quality assurance program.

The effective control of postoperative pain is important and necessary not only for patient comfort but also for rapid recovery and optimal results. The effectiveness of newer methods such as patient-controlled analgesia and intraspinal techniques and the availability of newer, more potent, nonsteroidal anti-inflammatory drugs permit far more effective management of postoperative pain than with traditional intramuscular therapy.

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Perioperative Myocardial Ischemia

DESPITE RECENT ADVANCES in the diagnosis and treatment of coronary artery disease, the incidence of perioperative cardiac morbidity remains high. As a result, considerable research has been devoted to investigating perioperative myocardial ischemia as a possible reversible predictor of adverse surgical consequences.

Intraoperative electrocardiographic changes consistent with myocardial ischemia occur in 18% to 74% of patients with coronary artery disease who are having noncardiac operations. A recent study shows that ST segment changes occur laterally (V₄, V₅) and have a variable duration. Although intraoperative ischemia can be precipitated by increases in myocardial oxygen demand due to tachycardia and hypertension, 50% or more of the ischemic episodes may be unrelated to increases in indices of oxygen demand, suggesting that a primary decrease in the oxygen supply may be an important cause.

Although a previous study suggested that the occurrence of ischemia in the pre-bypass period in patients undergoing coronary artery bypass grafting may increase the risk of postoperative myocardial infarction, more recent studies show that a chronic pattern of ischemia exists preoperatively in patients having coronary artery bypass grafting as well as those having noncardiac surgical procedures. Furthermore, the intraoperative pattern of ischemia is no worse than the preoperative pattern, implying that anesthesia and surgery may not be as stressful as previously assumed and that the intraoperative pattern may simply recapitulate the ongoing preoperative pattern.

Finally, it is now established that postoperative ischemia is even more prevalent than ischemia occurring before or during an operation and is the most important predictor of

adverse cardiac events in high-risk patients undergoing non-cardiac operations. In fact, postoperative myocardial ischemia as detected by Holter electrocardiographic monitoring confers a 9.2-fold increase in the odds of a cardiac event. No other clinical, historical, or perioperative variable was associated independently with adverse cardiac results, including the cardiac risk index, a history of previous myocardial infarction or congestive heart failure, or the occurrence of ischemia before or during an operation. Accordingly, increased attention and resources should be focused on the postoperative period. Clinical trials of perioperative anti-ischemic therapies are currently under way. The results from these trials will determine whether the incidence of perioperative cardiac morbidity can be reduced by the prevention of postoperative ischemia.

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Sedating Patients in Intensive Care Units

ANXIETY, SLEEP DEPRIVATION, and pain are extremely common problems in patients in intensive care units and can lead to delusions, delirium, or psychosis. The neuroendocrine stress responses often associated with noxious conditions can produce deleterious hemodynamic, metabolic, nutritional, and immunologic changes. Inadequate control of any of these problems frequently results in unnecessarily large doses of sedatives. Coughing with an endotracheal tube and fighting the ventilator complicate the management of patients on ventilatory support. Asynchrony between spontaneous ventilatory efforts and mechanical breaths predisposes patients to pulmonary barotrauma, interferes with alveolar gas exchange, and increases the work of breathing. Neuromuscular paralysis for the control of inappropriate (central) hyperventilation mandates that sedation also provide amnesia.

Older sedation practices relied primarily on intermittent intravenous doses of morphine sulfate or meperidine hydrochloride. Diazepam or pentobarbital was given when amnesia or hypnosis was required. Unfortunately, boluses of these long-acting agents often caused serious circulatory and respiratory depression, and the high doses of opiates decreased gastrointestinal motility and prolonged ileus.

Midazolam hydrochloride, a short-acting benzodiazepine, has a pharmacokinetic profile that readily allows titration to effect when given by continuous intravenous infusion. Loading is best achieved by 0.5-mg increments followed by an infusion of 0.015 to 0.2 mg per kg per hour. Respiratory or circulatory depression is generally minimal, and even after prolonged infusions its effects usually dissipate within two hours after the infusion is stopped. The latter facilitates a rapid weaning from mechanical ventilation and neurologic evaluation. Withdrawal symptoms are uncommon, but tolerance may develop in some patients.

Supplementing midazolam is important whenever a patient has substantial pain, is on a ventilator, or tolerance develops. A concomitant infusion of an opioid or ketamine

hydrochloride augments the sedation, provides analgesia, and reduces drug requirements. Adding fentanyl citrate, 0.5 to 2 μg per kg per hour, sufentanil citrate, 0.05 to 0.2 μg per kg per hour, or alfentanil hydrochloride, 5 to 20 μg per kg per hour, can produce excellent analgesia and reduces midazolam requirements. Alternatively, ketamine, 0.15 to 0.5 mg per kg per hour, can also provide powerful analgesia. Unlike opioids, ketamine is a bronchodilator and mild respiratory stimulant. Psychotomimetic reactions, such as hallucination and nightmares, are uncommon when ketamine is combined with a benzodiazepine.

Propofol, a short-acting intravenous anesthetic with a rapid onset and termination, is an excellent sedative at low doses—1 to 6 mg per kg per hour. Dose-dependent respiratory depression and hypotension can be observed after administering a bolus but are generally minimal when propofol is given by infusion at this dose range. Propofol's principal advantage is that its effects usually dissipate within 15 to 20 minutes after the infusion is stopped. Withdrawal symptoms have been reported following prolonged propofol infusion.

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Perioperative Temperature Control

HUMANS NORMALLY MAINTAIN a core body temperature near 37°C. This temperature is maintained because deviations of only a few tenths of a degree trigger thermoregulatory responses, including vasoconstriction, shivering, active vasodilation, and sweating. General anesthetics profoundly impair normal thermoregulatory processing. For example, the core temperature triggering vasoconstriction is decreased from about 37°C to about 34°C by halothane, nitrous oxide and fentanyl citrate, nitrous oxide and propofol, and isoflurane. The exact triggering threshold depends on the anesthetic type and dose, but is similar in infants, children, and adults. In contrast, the core temperature triggering sweating and active vasodilation is increased about a degree by surgical concentrations of isoflurane and enflurane. The interthreshold range (core temperature not triggering thermoregulatory responses) thus is increased by general anesthesia from about 0.6°C to about 4°C.

Most patients become hypothermic during surgical procedures, and hypothermia usually develops in three distinct phases. During the first hour, the core temperature decreases about 1°C. Surprisingly, undressing patients in a cold room and washing their skin with fluid that is subsequently allowed to evaporate contributes little to the hypothermia. Anesthetic-induced vasodilation only minimally increases heat loss from the skin surface. Similarly, inducing anesthesia only minimally reduces metabolic heat production. Core hypothermia actually results because vasodilation allows heat in warm core tissues to escape into the cooler peripheral thermal compartment. This reduces the core temperature, increases the peripheral temperature, and leaves the body heat content unchanged.